REMARKS

Claims 28, 30, and 32 are pending in the present application.

At the outset, Applicants would like to thank Examiner Hines for the indication that the indefiniteness rejection and the obviousness rejection over Thomas et al have been withdrawn (October 19, 2004 Office Action, page 2, paragraph 2). Applicants also wish to thank the Examiner for the indication that Claims 30 and 32 have been allowed (October 19, 2004 Office Action, page 5, paragraph 5). Reconsideration of the outstanding rejection is requested in view of the remarks herein.

The rejection of Claim 28 under 35 U.S.C. §103(a) over Thomas et al in view of Gibbons is respectfully traversed.

The present invention provides, *inter alia*, an agglutination immunoassay comprising:

(a) preparing a nucleic acid-bound polypeptide by binding a nucleic acid to said polypeptide through a nucleic acid-binding motif in said polypeptide, and fixing said nucleic acid-bound polypeptide on the surface of particles;

(b) contacting the particles obtained in (a) with a sample, wherein said sample may contain an antibody to an antigen, wherein said antigen is said polypeptide fixed on the surface of solid particles; and

(c) measuring agglutination images of said particles caused by formation of antigen-antibody complex

wherein said nucleic acid is bound to at least one terminus of said polypeptide, and

wherein said nucleic acid-bound polypeptide further comprises a nucleic acid-binding motif through which said nucleic acid is bound to at least one terminus of said polypeptide (Claim 28). The cited art of record makes no disclosure or suggestion of the foregoing claimed invention, much less realize the unexpected results flowing therefrom.

Based on the foregoing, it is clear that the present invention assays an antibody that binds to a polypeptide antigen. To measure the antibody by agglutination immunoassay *the polypeptide antigen/nucleic acid complex is fixed to particles*. By using the particles upon which the polypeptide antigen/nucleic acid complex is fixed, the antibody binding to the polypeptide antigen is measured. Therefore, the polypeptide antigen/nucleic acid complex on the particles are used as the reagent for the immunoassay and in the claimed method the object to be measured is the antibody, not the polypeptide antigen/nucleic acid complex.

As such, the immunoassay of the present invention represents a deviation from the usual agglutination immunoassay. In the usual agglutination immunoassay for measuring antibodies, the polypeptide antigen for which the antibody is directed is fixed on particles. The state of the art at the time of the present invention believed that it would not make sense to fix the polypeptide antigen/nucleic acid complex to particles rather than just the antigen, because the nucleic acid does not participate in the antigen-antibody interaction. Surprisingly and unexpectedly, the present inventors have determined that by fixing the polypeptide antigen/nucleic acid complex rather than just the antigen itself, the sensitivity of the immunoassay may be significantly enhanced. This is shown in Example 5 and Table 2 appearing in the present specification.

In these experiments, by using the particles on which the polypeptide antigen/nucleic acid complex is fixed, the antibody in the antisera was measured. In contrast, when the

particles only contained the antigen fixed thereto, the antibody in the antisera could not be measured. Similarly when a monoclonal antibody was measured, the sensitivity of the immunoassay having the polypeptide antigen/nucleic acid complex fixed to the particles was greater than that of the corresponding immunoassay in which only the antigen was fixed to the particles.

None of Thomas et al, Gibbons, or the combination thereof, discloses or suggests the foregoing. Thus, these references cannot affect patentability of the claimed invention.

Thomas et al disclose a general method for detecting and measuring analytes in a sample. However, Thomas et al are silent as to measurement of an antibody using the particles upon which a polypeptide antigen/nucleic acid complex has been fixed. The Examiner points to column 8, lines 60-65 as reciting specific DNA/protein interaction; however, this disclosure is unrelated to the present invention because the polypeptide/DNA complex is fixed on particles in the present invention, but isn't in Thomas et al. Further, in contrast to Thomas et al, in the present invention the antibody is measured as it interacts with the binary polypeptide antigen/nucleic acid complex, which was fixed to particles. Thomas et al is measuring the interaction between the polypeptide and the DNA. Applicants note that these are unrelated parameters.

Further, the Examiner points to Example E of Thomas et al, which is directed to the measurement of p19 bound to RSV-RNA. The Examiner asserts that an anti-p19 antibody is used in this example; however, Applicants wish to note that Example E of Thomas et al measures the p19/RSV-RNA complex by measuring using the anti-p19 antibody. Thus, what is measured in Thomas et al is the p19/RSV-RNA complex and not the anti-p19 antibody. Accordingly, the disclosure of Thomas et al is distinct from the presently claimed method.

Moreover, even if the artisan would glean a suggestion to measure the antibody from the disclosure of Thomas et al, this disclosure fails to disclose or suggest the aforementioned unexpected advantages flowing from the claimed invention.

The Examiner cites Gibbons as disclosing a general method for an agglutination immunoassay. However, Gibbons fails to disclose or suggest measuring an antibody using the particles upon which a polypeptide antigen/nucleic acid complex has been fixed as presently claimed. As such, Gibbons fails to compensate for the deficiencies discussed above for Thomas et al.

Further, even if the artisan were to combine the disclosures of Thomas et al and Gibbons, there would be no expectation engendered by these disclosures of the unexpectedly superior effects of the present invention, namely enhanced sensitivity. As such, Applicants submit that the disclosures of Thomas et al and Gibbons fail to support even a *prima facie* case of obviousness. Moreover, even if the Examiner were to somehow assert that a *prima facie* case of obviousness does exist such a rejection should be rebutted by the unexpected results shown in Example 5 and Table 2 of the present specification.

In view of the foregoing, withdrawal of this ground of rejection is requested.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

Vincent K. Shier, Ph.D.
Registration No. 50,552

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413-2220
(OSMMN 08/03)
NFO:VKS